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Principles of Pain Management

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RELATIONSHIP DISCLOSURE:
Dr Hogans has received intellectual property interests from a discovery or technology relating to health care and publishing royalties from publications relating to health care. Dr Hogans has noncompensated relationships as a grant reviewer with the National Institutes of Health (NIH) and the Veterans Affairs (VA) Office of Research and Development and as a director-at-large with the American Academy of Pain Medicine that are relevant to American Academy of Neurology (AAN) interests or activities. The institution of Dr Hogans has received research support from the VA Office of Research and Development.

UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Hogans discusses the use of several pain-active antidepressants and antiseizure medications, none of which are approved by the US Food and Drug Administration (FDA) for the management of pain.

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ABSTRACT

OBJECTIVE: This article introduces the general principles of assessing, diagnosing, and managing pain relevant to neurologic practice.

LATEST DEVELOPMENTS: Scientific understanding of and clinical practices related to pain and pain management are advancing. The field is remarkable for the diversity of health professions engaged in this effort, including physicians, scientists, psychologists, pharmacists, and many others. Pain classification is transforming with pending changes to the *International Classification of Diseases* diagnostic coding system, and pain assessment has moved toward consistent application of the biopsychosocial model. The diagnosis of pain has continued to become more sophisticated with the development of additional testing modalities, clearer classification systems, and diagnostic criteria. Pain management requires both pharmacologic and nonpharmacologic elements; systematic review evidence for both of these and interventional and surgical management are increasingly available. The context of treatment remains important given the impact of social determinants of health and limitations of access to diagnostic and treatment resources. Due to global and interprofessional collaborations as well as new research funding, the outlook is positive.

ESSENTIAL POINTS: Pain is a protean experience for humans; functional MRI (fMRI) and other research modalities show that pain perception is highly multifocal, and modulation occurs at many nervous system levels. Neurologists bring special skills to pain evaluation and management, are well equipped to appreciate both the focal and diffuse nature of pain, and can envision how pain attenuates sleep, cognitive function, mobility, motivation, and social connection. By operationalizing expert knowledge of the nervous system, implementing relevant therapies, and collaborating with diverse health professions to manage pain, neurologists can succeed at and find meaning in optimizing patient outcomes.

INTRODUCTION

Pain-associated conditions are highly prevalent in neurology and include headache and orofacial pain, spinal disorders such as cervicalgia and lumbar radiculopathy, neuropathic disorders such as diabetic peripheral neuropathy and postherpetic neuralgia, and pain syndromes that arise in the context of other neurologic conditions

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such as multiple sclerosis.[1] Arguably, all pain-associated conditions are of interest to neurologists as all pain is neurally mediated; however, the enrollment of neurologists in pain fellowship training programs remains sparse. This article addresses the general principles of pain assessment, diagnosis, and management and the context of treatment, highlighting some broad developments in pain science and clinical practice. The classification and basic terminology of pain-associated conditions continue to evolve, and several commonly used pain terms are highlighted in TABLE 1-1[2-21] along with selected caveats and limitations.[13,22,23]

PAIN CLASSIFICATION, TERMINOLOGY, AND APPROACH

The diagnostic classification of pain is best exemplified by the systematic classification of facial pain and headache disorders found in the International Classification of Headache Disorders (ICHD), which allows for relatively detailed diagnoses of these disorders in both inpatient and outpatient neurology settings that are consistent from one location to another.[24] The development of headache and facial pain diagnostic nosology reflects the efforts of Arnold Friedman and colleagues[25] who published an initial classification framework in 1962. The ICHD was first published in 1988 and subsequent editions have responded to advances in science and clinical practice.[25] The advantage of having a unified approach to headache and facial pain diagnosis is that, although there are many different types of headache and facial pains and all are principally subjective, there is a specific set of standards on which to base the diagnosis of each disorder. This approach to diagnosis and classification has further advanced pain research as specific mechanisms and disorder-specific treatments have been developed and tested.[26-28] The ICHD can be viewed online without a subscription and is a useful resource for students, residents, and nonspecialists. The current version is harmonized with the version of the *International Classification of Diseases (ICD)* available at the time of publication.[29] Neurologic management of headache and facial pain shares features with the management of other forms of pain including a focus on attending to and acknowledging the patient's experience of pain and related symptoms, seeking diagnostic information through neurologic examination and diagnostic testing, and integrative management including pharmacologic and nonpharmacologic therapies, potentially incorporating lifestyle modifications using a "whole-health" approach and interprofessional collaboration.[30,31]

Pain-associated spine disorders are highly prevalent in neurology practice.[8,32,33] At present, disorders of the spine are not systematically diagnosed and classified in the same manner as headache disorders.[34-37] There is no widely recognized and accepted universal classification scheme for spine disorders, and the most cited articles addressing low back pain support a reductionist approach, instructing generalists to classify most low back pain as nonspecific and screen for red flags (although a consensus on red flags does not exist) and to advise patients to remain active and take over-the-counter analgesics.[34,38-41] Because neurologists have expertise in neurologic localization and diagnosis, spine pain guidelines intended for generalist practice will not be comprehensive and further diagnostic discernment is generally required.[42] Neurologists can identify focal neurologic deficits and emergently manage both common and potentially catastrophic neurologic

KEY POINTS

- The systematic classification of facial pain and headache disorders in the International Classification of Headache Disorders allows for relatively detailed diagnoses of these disorders in both inpatient and outpatient neurology settings that are consistent from one location to another.
- The neurologic management of headache and facial pain includes acknowledging the patient's experience of pain and related symptoms; seeking diagnostic information through neurologic examination and diagnostic testing; and integrative management including pharmacologic and nonpharmacologic therapies, potentially incorporating lifestyle modifications using a "whole-health" approach and interprofessional collaboration.

disorders.[42-45] This capability is consistent with neurologic training and scope of practice, and in many instances, neurologists will recognize specific syndromes and conditions relating to spinal pathology, as illustrated in CASE 1-1.[35,44] The classification of pain in the setting of spinal cord injury is one example of how pain classification can both support patient care and advance broader understanding by carefully parsing the origins of pain in a manner that reflects both pain mechanisms and therapeutic needs.[46] Pathologic processes giving rise to spine pain can be biomechanical, musculoskeletal, neuropathic, nociplastic, central sensitization mediated, infectious, and immune mediated. In

TABLE 1-1 **Frequently Referenced Definitions in Pain**

Term	Definition	Limitations and concerns
Pain	"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."[2]	The current definition may not acknowledge a patient's experience of pain feeling akin to "tissue damage" and may not sufficiently incorporate psychosocial factors[2]
Nociceptive pain	"Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors."[3]	This raises the question of whether pain experienced acutely from nerve damage is truly neuropathic or nociceptive
Neuropathic pain	"Neuropathic pain can be defined as a process occurring after a primary lesion or disease of the somatosensory nervous system."[4]	The prior IASP definition included "dysfunction" as well as disease By excluding dysfunction and focusing on demonstrable lesions, molecular, microscopic, and "as yet to be defined" neuropathic changes are excluded[5]
Inflammatory pain	"...associated with tissue injury and infections, results from the heightened sensitivity of the peripheral terminals of nociceptor sensory neurons in response to exposure to inflammatory mediators."[6,7]	By many measures, inflammatory pain accounts for the vast majority of pain globally; nonetheless, the IASP currently excludes this mechanism[8,9]
Nociplastic pain	"Altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain."[10]	Newer term; not well validated; the definition of "actual or threatened tissue damage" is constrained by clinical resources and expertise[11]; potentially excludes overlap with other pain forms
Allodynia	"Pain due to a stimulus that does not normally provoke pain."[3] "Pain caused by a normally non-painful stimulus."[12]	Note that this is a pain response not typical of normal nociceptive processing
Hyperalgesia	"Increased pain from a stimulus that normally provokes pain"[3] "A heightened experience of pain caused by a noxious stimulus."[12]	Note that this is a pain response not typical of normal nociceptive processing

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general neurologic practice, which includes urgent and emergent hospital consultations, cases of spinal cord disorders presenting with prominent pain may lead to death, paralysis, or permanent disability, and focal neurologic findings can herald dire outcomes if the underlying syndromes (eg, infection, tumor, stroke of the spinal column) go unaddressed.[43] For example, Guillain-Barré syndrome, the most common sporadic form of paralysis, can present in urgent care settings with acutely developing diffuse low back pain and may initially manifest with only subtle decreases in muscle stretch reflexes and mild weakness, yet evolve to apnea within hours.[47]

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Term	Definition	Limitations and concerns
Hypoalgesia	"Diminished pain in response to a normally painful stimulus."[3] "A decreased perception of pain caused by a noxious stimulus."[12]	Note that this is a pain response not typical of normal nociceptive processing
Chronic pain	"Pain that persists or recurs for more than 3 months" or pain which persists beyond the time required for normal healing to occur.[13]	The IASP definition excludes the possibility that normal healing time would exceed 3 months, which could be normal for some conditions (eg, complex spine surgery)
Breakthrough pain	Most commonly used in the context of cancer pain management "A flare of pain that might happen even though you are taking pain medicine regularly for chronic pain" (lay definition)[14] "Episode of severe transient pain in patients with cancer"[15]	The application of cancer pain management principles to the treatment of chronic noncancer pain has not been validated and may have contributed to the US opioid epidemic and ensuing corrections[16]
Central sensitization	"Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input."[3] "An amplification of neural signalling [sic] within the central nervous system that elicits pain hypersensitivity"[17]	Incorporates multiple mechanisms (eg, long-term potentiation, glial activation, sprouting, phenotypic switching), none of which are currently confirmable using widely available clinical tests
Central sensitivity syndromes and chronic overlapping pain conditions	Prevalent chronic pain conditions which may coexist in specific individuals; conditions include migraine; chronic tension-type headache, temporomandibular joint disorder, chronic low back pain, urological, pelvic, and gynecological pain disorders, irritable bowel syndrome, and fibromyalgia[18]	These conditions have increased risks for sleep disturbance including obstructive sleep apnea, fatigue, and selected psychological features[19,20] There is considerable overlap between the set of conditions termed *central sensitivity syndromes* and those termed *chronic overlapping pain conditions*
Opioid-induced hyperalgesia	"Nociceptive sensitization following acute or chronic exposure to opioids."[21]	Note that multiple mechanisms are potentially included here including active opioid exposure, withdrawal, and persistent hyperalgesia following long-term cessation

CASE 1-1

A 47-year-old woman underwent right shoulder surgery, and upon awakening reported acute low back pain. A neurology consultation was requested, and the patient described mild dull pain at rest that became sharp with rolling over in bed, sit-to-stand, and attempts at ambulation. The patient pointed to the maximal pain area with one finger (left low back at the L5 disk level, 2 to 3 inches lateral of midline) but indicated that the pain radiated "all over" the buttock. She had no prior history, although she acknowledged years of intermittent mild-to-moderate axial low back pain following exertion such as lifting heavy objects. She noted that the current pain was so severe that she was nauseous and had an urge to defecate when standing. Having recently moved to the area, she felt unsure about managing her pain at home.

Examination revealed a body mass index of 28.4 and intact mental status, cranial nerves, sensation, and reflexes. Her upper extremity coordination and strength were normal except for limitations due to the recent surgery. A lower extremity motor examination showed full strength on the right with mild guarding upon hip testing; her left leg showed full strength except for antalgic guarding on hip testing. Palpation testing demonstrated tenderness without evident mass or swelling over the area of the left rostral sacroiliac joint. Straight leg testing showed an equivocal result with pain radiating to the buttock on the left and mild guarding on the right. Plain-film radiography of the lumbosacral spine demonstrated minimal spondylosis. Due to the absence of neurologic deficits, referral to a pain medicine specialist was contemplated; however, no immediate consultation was available and there was a 3-week wait for pain clinic appointments.

Sacroiliac joint dislocation resulting from asymmetrical loading was suspected based on the history and presentation and was confirmed by the examination. As the patient was still recovering from her surgery, a physical therapist was consulted to provide bedside manual manipulation. Cold packs were applied 3 times a day for pain relief.

COMMENT

This case exemplifies the importance of interdisciplinary collaboration in the diagnosis and treatment of neurologic pain. In addition, this case demonstrates that musculoskeletal conditions, which involve mechanisms of nociceptive and inflammatory pain, may present with radiating pain and be interpreted as neurologic by non-neurologists. Conditions like this are nonetheless profoundly impactful in terms of producing severe pain and motor dysfunction. The differential diagnosis included radiculopathy and other nerve injuries, and thus neurology was consulted; however, the neurologist suspected sacroiliac joint dislocation. Knowing the basic diagnosis and management of common conditions in the pain differential diagnosis can spare patients from unnecessary treatment delays.

Current pain categorization systems generally organize pain into one of four domains: nociceptive pain, neuropathic pain, inflammatory pain, and nociplastic pain. Nociceptive pain is caused by tissue injury or trauma. Neuropathic pain is caused by disease or dysfunction of the nervous system. Inflammatory pain is associated with phenotypic changes in afferent neurons mediated by inflammatory mediators, resulting in increased sensitivity to painful and nonpainful stimuli. Nociplastic pain is a relatively recent construct defined as pain reflecting central sensitization. The following sections describe neuropathic and nociplastic pain.

KEY POINTS

- Pathologic processes giving rise to spine pain can be biomechanical, musculoskeletal, neuropathic, nociplastic, central sensitization mediated, infectious, and immune mediated.
- Common neuropathic pain patterns include a distal symmetrical gradient-type pattern, neuropathy affecting only small fibers (typically diffusely distributed), "named nerve" patterns, radicular (dermatomal) patterns, and visceral involvement patterns.

NEUROPATHIC PAIN

Neuropathic pain takes several forms but almost all relate to a disease or dysfunction of the nervous system.[22,31,45,48-52] Although recent revisions to the International Association for the Study of Pain (IASP) definition of neuropathic pain have emphasized demonstrable lesions of the nervous system, this definition may have more utility in research settings than in clinical practice.[53] The IASP currently endorses that "[a] suspected diagnosis of neuropathic pain requires specific investigations to ascertain that the pain originates in the nervous system."[12,22] Whether such investigations involve only a systematic neurologic examination or necessitate "objective testing" depends on provider expertise, clinical circumstances, and the availability of specific resources.[48,52] For example, the diagnosis of small fiber neuropathy has been constrained by limited access to expert clinicians and skin biopsy staining for epidermal nerve fibers or quantitative sensory testing.[51,52] Clinically, neuropathic pain disorders are often most effectively classified in terms of etiology, as this will determine the treatment approach; however, at the time of first presentation, the etiology may not be established.[45,46,48,51,52] Pattern recognition is an important tool for the assessment of a patient with any form of pain, as establishing the neuroanatomic distribution of positive and negative symptoms and signs is key to unlocking the differential diagnosis.

Common neuropathic pain patterns include a distal symmetrical gradient-type pattern, neuropathy affecting only small fibers (typically diffusely distributed), "named nerve" patterns which demonstrate clear delineation between normal and abnormal areas, radicular (dermatomal) patterns, and visceral involvement patterns.[42-44] Other regional pain patterns that are important for the differential diagnosis but are not specifically neuropathic include the patterns associated with muscle injury, bone injury (ie, sclerotomes), ligamentous and tendinous strain, disk injury (ie, diskogenic pain), and multicentric patterns such as diffuse enthesopathy (related to vitamin D deficiency), osteogenic syndromes, and fibromyalgia.[54-56] It is difficult to overemphasize the importance of pain patterns in the differential diagnosis of pain, and it is important to recognize that neuropathic and non-neuropathic pain syndromes have stereotypical and nontypical patterns of pain signs and symptoms.

CENTRAL SENSITIZATION, NOCIPLASTIC PAIN, AND SYNDROMES OF ABERRANT PAIN SIGNALING

There is debate over whether central sensitization represents a form of neuropathic pain. This is important conceptually as the underlying pathologic processes will ultimately determine the nature of the definitive treatments,

which are yet to enter the clinical armamentarium. The debate arose from a decision by the IASP to redefine neuropathic pain to only include conditions that have a demonstrable lesion (ie, provable through imaging or neurophysiology) and exclude conditions that are traceable to a neurochemical, molecular, or microscopic cause. No well-established clinical tests are currently used to determine the presence of central sensitization, which can manifest from one or more underlying pathophysiologic processes, including long-term potentiation, phenotypic reorganization, central axonal sprouting, proliferation of microglia, and glial sensitization. This will be an area of evolving practice refinement in the next decade.[17,57,58]

The initiative to apply the term *nociplastic* to certain forms of pain is a relatively new development that is not reflected in the current version of the *ICD* system and that continues to undergo definitional development. Several recognized syndromes may reflect processes related to central sensitization and may include the highly prevalent tension-type headache; chronic overlapping pain conditions, which include temporomandibular joint disorder, dysmenorrhea, and irritable bowel syndrome; complex regional pain syndrome types I and II; and widespread pain syndromes, which include fibromyalgia.[59,60] For more information on several syndromes related to central sensitization, refer to the article "Chronic Widespread Pain" by Narayan R. Kissoon, MD,[61] in this issue of *Continuum*.

Both clinical and basic science evidence suggests that the current scheme overlooks the effects of inflammation (eg, osteoarthritis) in inducing persistent phenotypic changes in somatosensory elements as a mechanism working in concert with neuropathic processing alterations.[6,10,11,22,23,62,63] Some authors refer to this as inflammatory pain, whereas others incorporate this into the nociplastic category. Nociceptive pain is associated with acute injury or trauma, and some syndromes involve recurrent acute trauma at macroscopic or microscopic levels (eg, spondylolisthesis, sacroiliac joint dysfunction, other joint instability syndromes). Given the frequency with which patients with complex pain conditions are encountered in clinical practice, neurologists need to know that several pain mechanisms may be active at any phase of treatment. Rational pain therapy incorporating agents and therapies to address nociceptive, inflammatory, and neuropathic pain may necessitate the use of polypharmacy and multiple nonpharmacologic therapies to successfully manage complex pain conditions, especially spine-related pain conditions and other orthopedic conditions with compressive peripheral nerve involvement (ie, Ehlers-Danlos syndrome).

Other neurologic syndromes demonstrate high rates of pain. People with traumatic brain injury and multiple sclerosis are especially likely to experience persistent pain, whether from headache, cervical syndromes, or other pain processes.[64] People with Parkinson disease have increased rates of pain diagnoses and, although the association of pain with specific dementias is not well defined, the management of pain in the context of dementia is more complex. Conditions such as motor neuron disease and muscle diseases are often associated with pain. Polymyalgia rheumatica and giant cell arteritis are often associated with shoulder girdle and hip girdle pain as part of the syndrome.[24]

The management of pain-associated conditions in neurologic practice may be iterative. Establishing a firm diagnosis may require testing; for this reason, it is

often necessary to initiate symptomatic treatment concurrently with the diagnostic workup so that patients do not continue to experience uncontrolled pain while awaiting test results. This is referred to as the *parallel path model*, which envisions assessment and symptomatic treatment occurring in a coordinated, concurrent manner.[65]

Pain is a highly active area of research and related activity. Recent key developments include a revised IASP definition of pain and other aspects of pain including a definition of neuropathic pain, developed primarily as a research tool.[12,13,22,23] The mandatory adoption of the tenth edition of the *ICD* (*ICD-10*) in late 2016 was followed by several revisions to the *ICD-10* codes available, and stakeholder work for the upcoming eleventh edition of the *ICD* (*ICD-11*) has been completed.[66] The new classification system will require a major revision to coding practices as practitioners will be expected to distinguish both pain mechanisms and underlying pathologies. With the *ICD-11* system, providers will be expected to distinguish chronic primary musculoskeletal pain from chronic secondary musculoskeletal pain, even though the distinction between these is unclear and subject to considerable controversy.[23] From a neurologic viewpoint, it is not clear what a chronic primary musculoskeletal pain condition would be as primary pain conditions are understood to arise directly from disease or dysfunction of the pain system itself, whereas the musculoskeletal system is principally a structural and locomotor system.[10] Chronic neuropathic pain is not specified as a "secondary pain" but is shown consistently in diagrams colocated with other secondary pain diagnoses.[22,66] There will also be codes for distinguishing "central" from "peripheral" neuropathic pain, a potentially false dichotomy that may exceed the bounds of clinical discernment, as peripheral nociceptive, inflammatory, and neuropathic processes can and will result in central sensitization.[17,67]

Pain research will continue to improve practice and patient experience. In the realm of nociceptive pain, the enhanced postoperative recovery programs system of formalized quality improvements in perioperative care has resulted in dramatic reductions in pain during and following surgery as well as marked decreases in opioid dispensing in the context of operative management.[68,69] Federal research and industry-sponsored studies continue to generate new therapeutic approaches as well as improved implementation and delivery of existing treatments.[70] Patient and caregiver engagement requires the readiness of health care professionals to use the frameworks of "whole health," shared decision making, motivational interviewing, a therapeutic alliance, and other evolving frameworks that, taken together, will further improve pain-focused neurologic care.[71]

ASSESSMENT

Neurologic appraisal may be instrumental in attaining a clear diagnosis and treatment plan for many patients with pain. Neurologic history taking and examination typically focus on describing and delineating areas of neural function and dysfunction in both the central and peripheral nervous systems,[43] and almost universally, the process of history taking is essential to defining a pain-associated condition.[72,73] Features of pain presentation of particular interest include symptom quality, region, severity, and timing, as well as identifying factors that alleviate and worsen symptoms (**TABLE 1-2**).[74]

KEY POINTS

- There are no well-established clinical tests currently used to determine the presence of central sensitization.
- Given the frequency with which patients with complex pain conditions are encountered in clinical practice, neurologists need to know that several pain mechanisms may be active at any phase of treatment.
- It is often necessary to initiate symptomatic pain treatment concurrently with the diagnostic workup so that patients do not continue to experience uncontrolled pain while awaiting test results.
- New pain classification systems will require a major revision to coding practices as practitioners will be expected to distinguish both pain mechanisms and underlying pathologies.
- Features of pain presentation of particular interest include symptom quality, region, severity, and timing, as well as identifying factors that alleviate and worsen the symptoms.
- In the diagnosis of pain-associated conditions, there is a role for the assessment of musculoskeletal dysfunction.

Patients with chronic pain will often have multiple pain areas or diagnoses. Optimally, the clinician characterizes each of these, at least in part, to ascertain whether they represent separate processes or a single phenomenon such as a chronic widespread pain syndrome (a form of chronic primary pain in the *ICD-11* classification system).[13]

Neurologic examination is crucial to informing a pain diagnosis. In many cases, the sensory examination may take precedence, especially when neuropathic pain is suspected, with motor, cerebellar, and autonomic features taking on a confirmatory role.[44] In the diagnosis of pain-associated conditions, there is a role for the incorporation of musculoskeletal dysfunction assessment.[74] For example, appraising spine pain may require an assessment of range of motion and provocative tests, headache may require palpation of the head and neck as well as range of motion, and neuropathy testing may require an assessment of pulses and peripheral edema.[47,75]

Clinical reasoning in the context of pain-associated conditions may prioritize findings and symptoms arising from the sensory system. This contrasts with other disorders where sensation is often viewed as confirmatory. In assessing and diagnosing patients with pain-associated conditions, the primary focus will be on the perceptions of pain and other sensory inputs, contrasting small fiber

TABLE 1-2

Features of a Pain-focused History and Physical

Quality of symptoms

- Includes descriptors such as burning or aching
- May guide the distinction between neuropathic and non-neuropathic pain

Region of symptoms and signs

- May include neurologic patterns (eg, radicular, dermatomal, hemisensory, radiating, diffuse)
- May also include non-neurologic patterns (eg, sclerotomal)

Severity

- Most often defined as relating to pain intensity
- Pain intensity communicated using a 0 to 10 (11-point) numerical rating scale
- Pain intensity shows high variability between individuals
- Pain intensity ratings are often highly reproducible for individuals in research settings
- Pain intensity ratings may worsen (ie, a mild stimulus will produce more pain) with chronic pain
- Pain intensity ratings may improve or worsen (ie, increase or decrease in response to a fixed stimulus) with psychosocial factors
- Pain intensity assessment with a numerical rating scale is exceptionally rapid and feasible for those with low literacy
- Pain interference is the extent to which pain interferes with activity (eg, sleep, enjoyment)
- Pain-related distress is the affective aspects of pain (eg, suffering)

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functions of heat, cold, and pain sensation as well as itch and efferent small fiber functions (eg, focal erythema) with large fiber functions of proprioception and vibration which may or not be involved, depending on the etiology.[48,51,76] It is important to recognize that pain may have impacts on motor, cerebellar, and cognitive function, but these will vary by etiology and, while presenting management issues, will be findings that are confirmatory in nature.

Patient characteristics have a modest impact on clinical pain reasoning, with some exceptions. Some conditions are far more prevalent in older adults than those typical of pediatric or middle-aged patients.[1,56] While some conditions pertain to primary and secondary sex organs, male-female differences in pain prevalence are small. Populations facing socioeconomic and social disparities do demonstrate some variability in rates of pain conditions, but epidemiologically, access to care is a major barrier, and once care is accessed the focus should be on providing excellent quality care to each patient.[77] Pain can present in patients from any demographic group. Although there are groups with higher rates of specific pain-associated conditions, pain is so prevalent that because patients are evaluated as individuals in a clinical setting, it is typically not possible to exclude most pain diagnoses based on demographic features alone. For example, although studies based on clinic

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Timing

- Timing of pain and related symptoms is critically important to diagnosis
- Acute pain, especially with motor features, may necessitate emergent assessment
- Chronic pain: definition of *chronic* varies with underlying process
- Chronic pain is that exceeding "normal time for healing" (some use 3 months)
- Waxing and waning pattern of variation in pain may be informative
- With insidious pain, providers may need to revisit the initial diagnosis
- Breakthrough pain: often associated with cancer-related pain
- Breakthrough pain may also pertain to patients with stable, known chronic pain–associated conditions who experience concurrent development of a new condition
- Worsening pain may also reflect entering a progressive phase of chronic illness
- Timing is important for the management and selection of therapies

"Usually associated with"

- Association of pain with additional symptoms, such as rash, may illuminate diagnosis

"Very much better with"

- Alleviating factors can inform diagnosis
- Substantive relief with specific treatments or activity may guide treatment planning

"Worsened by"

- Aggravating factors are important for diagnosis and management
- Mitigation of aggravating factors may be important for sustaining vocational and avocational function

samples find that rates of fibromyalgia among female patients far exceed those in males, population-based symptom surveys indicate that sex differences are much smaller, suggesting that true prevalence differences may be smaller than commonly thought.[60,78,79] Tension-type headache is an example of a condition with remarkably high population prevalence that is relatively rare in the clinical setting, as most patients will self-manage uncomplicated tension-type headache.[80] Among older adults, there is a slight female predominance for most pain diagnoses, with the exception that diabetic peripheral neuropathy has a slight male predominance.[81]

Health systems vary in terms of both the opportunities for interprofessional collaborative care for patients with chronic pain and the provision of a broad range of therapies.[82,83] For patients with neuropathic pain, it is often appropriate to consider whether the neuropathic pain syndrome would benefit from the addition of physical or occupational therapies. Physical therapy can be especially important for older adults with length-dependent peripheral neuropathies where the risk for falls and ensuing orthopedic injuries is high.[84] For spinal disorders, there is consideration for collaborative care or referral to chiropractic, physical therapist, pain interventionalist, or surgical evaluation depending on the clinical presentation and the patient's preferences.[85] Few health systems have truly integrated care for persons with chronic pain, as these services tend to be highly resource intensive. The Veterans Health Administration is an example of a health system that prioritizes the engagement of prosthetics and offers a wide range of treatments including whole-health modalities such as exercise, nutrition, and mind-body therapies like yoga and qigong, while also offering mental health comanagement and specific clinical psychological therapeutic approaches such as cognitive behavioral therapy and acceptance and commitment therapy.[86]

Interprofessional collaboration is an important evolving approach for health care professionals who come to their work through separate professional training tracks. Long led by physicians, teams of health care workers are increasingly recognizing that team-oriented health care delivery can be more effective and satisfactory.[87,88] Even when health care cannot be delivered within a single integrated health system, interprofessional collaboration and the principles of teamwork, communication, ethics, and values, and the responsibility and roles of other professions can deliver care that is patient centered and responsive to the community's needs.[89] Some exposure to these approaches is helpful as we bridge communication gaps between professions, acknowledging the professional expertise of pharmacists, physical therapists, clinical psychologists, nurses, nurse practitioners, physician assistants, chaplains, and others as members of the health care team.[90] Finally, the patient, caregivers, and even support animals are important parts of the health system and team when addressing pain.[91] The use of motivational interviewing methods prepares neurologists and others to elicit patient values and priorities in the design of coordinated pain management plans (**FIGURE 1-1**).[92]

DIAGNOSIS

Diagnostic approaches to pain-associated conditions are distinct from those for other neurologic and neurally mediated conditions in terms of the focus on the somatosensory system and associated processes. Nociceptive processing, like all somatosensory signals, involves (1) transduction, the process of translating

external energy (eg, heat, cold, pressure) into action potentials; (2) transmission, which carries information from the peripheral sensing structures to the spinal and supraspinal centers; (3) modulation, which tempers the flow of information; and (4) perception, which for pain is highly multicentric. The exceptional features of nociceptive processing are delineated with selected clinical implications.[58,93,94]

The differential diagnosis is critically important to the evaluation process for patients with pain conditions, and the identification and localization of lesions of the nervous system are especially valuable in this regard. Often, non-neurologists may not be familiar with the innervation of a particular area and seemingly minor clues can yield important diagnostic information (eg, reflex asymmetry, focal weakness, autonomic aberrations).[76] The development of an appropriate differential diagnosis requires knowledge of the most relevant common conditions as well as those that are potentially catastrophic. When a condition presents that could be benign, problematic but self-resolving, or catastrophic, it is always important to weigh the potential harm to the patient of a missed catastrophic diagnosis. For example, new-onset midthoracic spine pain could be nonspecific "back" pain, ligamentous strain, shingles, a collapsed vertebra, or a spinal abscess; some of these are benign, while others present substantial peril. Through neurologic assessment and diagnostic reasoning, the neurologist's role is to discern the likelihood of needing time-sensitive and resource-intensive testing.

Diagnostic testing is driven by the conditions identified in the differential diagnosis, with special attention to those entities likely to be present, progressive, and harmful. When central nervous system conditions such as myelitis, tumors, infectious masses, or multiple sclerosis are suspected, MRI is typically necessary. For peripheral neuropathy, nerve conduction studies and EMG are most helpful unless there is evidence of only small fiber involvement to the exclusion of large fibers, as evidenced by exam findings of hypersensitivity to repeated presentation of sharp stimuli (eg, sharp-stick tapping test) in the context of

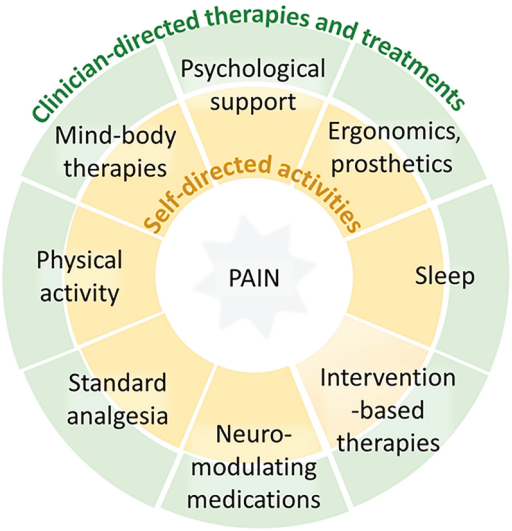

FIGURE 1-1
Coordination of pharmacologic and nonpharmacologic therapies in the management of pain. This model incorporates features of interprofessional collaboration and whole-health and rehabilitative approaches. The aim is to activate as many pain modulation mechanisms including endogenous pain modulation mechanisms (eg, endorphins and endocannabinoids) as feasible for patients with chronic pain, with the goal of restoring health through the modulation of pain in a patient-centered and practical manner. The pharmacologic and nonpharmacologic domains shown here can serve as a framework for a coordinated management plan. Motivational interviewing approaches are used to engage the patient in identifying self-directed health behaviors (*yellow bands*; eg, moderate physical activity) known to reduce pain and participation in clinician-directed therapies (*green bands*).

KEY POINTS

- **Pain may impact motor, cerebellar, and cognitive function, but these effects will vary by etiology.**
- **Health systems vary in terms of both the opportunities for interprofessional collaborative care for patients with chronic pain and the provision of a broad range of therapies.**
- **Interprofessional collaboration and the principles of teamwork, communication, ethics and values, and the responsibility and roles of other professions can deliver pain care that is patient-centered and responsive to the community's needs.**
- **Normal nociceptive processing, like all somatosensory signals, involves (1) transduction, the process of translating external energy (eg, heat, cold, pressure) into action potentials; (2) transmission, which carries information from the peripheral sensing structures to the spinal and supraspinal centers; (3) modulation, which tempers the flow of information; and (4) perception, which for pain is highly multicentric.**
- **The development of an appropriate differential diagnosis requires knowledge of the most relevant common pain-associated conditions as well as those that are potentially catastrophic.**

normal reflex, strength, vibratory, and proprioceptive findings. For small fiber neuropathy, skin biopsy testing for epidermal nerve fiber density is helpful, although some regional practice patterns favor quantitative sensory testing.[95] For these conditions, serologic, CSF, or other ancillary testing such as autonomic testing may be needed.

Spine pain–associated conditions may require various approaches to imaging depending on the duration, severity, and neurologic concomitants of the presentation. Plain x-rays (two or more views) can provide rapid information about conditions such as spinal fracture, dislocation (spondylolisthesis), spondylosis, and the general likelihood of disk degeneration; however, for more precise characterization of many persistent, neurologically involved, or progressive spine pain–associated conditions, MRI is needed to assess any compromised neural structures, and CT scan may be needed to further assess bony structures. For structural lesions, imaging is typically considered the definitive diagnostic test, although, in the context of suspected nerve or root compression, nerve conduction studies and EMG may be necessary to appraise functional impact. Plexopathies may require both nerve conduction studies and EMG and MRI to evaluate the plexus using MR neurography. Other testing may be required to either identify a lesion (eg, soft-tissue ultrasound) or evaluate elements included in the differential diagnosis (eg, vascular studies).

PSYCHOSOCIAL FACTORS

Psychosocial systems incorporating psychological, emotional, social, and sociological factors are especially important in pain. Psychosocial factors are often multiply present (eg, depression, trauma, and socioeconomic disadvantage occurring simultaneously). In addition, psychosocial factors have a profound impact on outcomes for patients with pain, so much so that over the last several years factors such as depression and a sedentary lifestyle have been strongly associated with several common pain syndromes, while persistent overexertion can also cause pain.[96] For many patients, one helpful approach is to invite the patient to identify the psychosocial factors that they believe are important to their current pain management. While this approach may not be appropriate for those with acute pain, when chronic pain is present, patients often have insightful perspectives on their own condition. One technique is to provide the patient with a list of common biological, psychological, and social factors observed in those with chronic pain and ask them to select those they believe are relevant. This both saves time and avoids unintended slights that may arise from asking about these items verbally.

In psychological terms, pain is a stressor that can result in decompensation in patients with both mild and serious mental illness. Substance use lapses and relapse behaviors may be exacerbated by trauma and posttraumatic stress disorder, and management may be complicated in the context of personality disorders.[97] Depression has a bidirectional relationship with pain in that pain increases the risk for depression and depression appears to increase the risk for chronic pain.[98] There is similarly a bidirectional relationship between anxiety and pain. Neurologists should be vigilant and diligent in screening for affective disorders and suicidality as the risk of suicide is increased for patients with chronic pain.[99] Substance use has a variable association with pain as nicotine and alcohol have limited impacts on pain diagnosis rates

(excluding headache); however, the prominent impact of opioids on pain processing and the profound reinforcement of opioids in terms of both pain relief and reward pathways means that in clinical practice opioid use disorder may have an outsized impact.[100-102] The relationships between pain, substance use, and affective disorders may be further complicated in the settings of trauma, polytrauma, sexual trauma, and posttraumatic stress disorder.[103,104] Personality disorders and certain personality types may be overrepresented in the population of people with chronic pain. Taken together, the interplay between psychological and chronic pain disorders requires neurologists to be prepared to rapidly engage in psychiatric or psychological comanagement, as well as have a standard operating procedure to ensure the safety of themselves and staff. Neurologists should have a low threshold for requesting a chaperone for a visit and should have no tolerance for abuse by patients or those accompanying patients.

Sleep also has a bidirectional relationship with pain in that even modest amounts of pain may worsen sleep quality and limit sleep duration; at the same time, poor quality and limited duration of sleep will limit patients' self-modulatory pain mechanisms.[105] There are many reasons to consider referral to a sleep clinic for patients with actively managed pain.

Social systems have a profound impact on the experience of pain. Employment, education, and economic status impact pain rates at the population level. At the individual level, neurologists can have the greatest impact by proactively inquiring about barriers to pain management in the workplace and providing support to overcome those barriers. These can take the form of ordering prosthetics or ergonomic equipment, completing Family Medical Leave Act paperwork to allow for a modified work schedule, ordering a period of light duty, coaching the patient to request an ergonomic workstation assessment, or engaging with the patient's functional capacity assessment process. Social support, social isolation, and caregivers have a major impact on outcomes and quality of life for people living with pain. Neurologists should assess and document the patient's social status and follow up consistently where relevant. Stages of life and major life events (eg, military service, schooling, work, aging) can impact a patient's experience of pain.[106] Neurologists should determine and respond to the work and home-life factors that influence a patient's capacity to manage pain. Aging, family, and independence are often major factors for how older adults approach living with chronic pain; utilizing techniques of motivational interviewing and acceptance and commitment therapy, which focuses on pursuing activities that have the greatest personal meaning, can be very helpful for prioritizing activities and selecting therapies.[92]

Disparities, stigma, and bias are central to the experience of pain; for example, patients with neuropathic foot pain often feel that people judge them because they have no physical signs of illness, but their feet hurt them terribly, destroying sleep quality and attenuating their confidence in ambulation. Social disparities and social stigma compound the suffering associated with pain. As noted above, sex has some impacts on pain diagnostic rates, but the experience of access to care or feeling believed and trusted as a patient can vary widely by sex and gender. Gender impacts pain processing, in terms of both psychosocial experience and in response to gender-affirming treatments.[107] Further study is needed to elucidate the mechanisms of these effects. Active and retired military

KEY POINTS

- For structural spine lesions, imaging is typically considered the definitive diagnostic test, although, in the context of suspected nerve or root compression, nerve conduction studies and EMG may be necessary to appraise functional impact.
- For many patients, a helpful approach is to invite the patient to identify the psychosocial factors that they believe are important to their current pain management.
- Neurologists should be vigilant and diligent in screening for affective disorders and suicidality as the risk for suicide is increased for patients with chronic pain.
- Even modest amounts of pain may worsen sleep quality and limit sleep duration; at the same time, poor quality and limited duration of sleep will limit patients' self-modulatory pain mechanisms.
- Motivational interviewing and acceptance and commitment therapy, which focuses on pursuing activities that have the greatest personal meaning, can be very helpful for prioritizing activities and selecting therapies for patients who have pain.

personnel and members of military families have high rates of direct and indirect experiences with pain.[108] Finally, access to health care and health care literacy have profound impacts on pain outcomes; persistent individual efforts, interprofessional collaboration, and community engagement may help to bridge these gaps.

Disability related to pain can be the most important aspect of a patient's experience of pain. For some patients, pain entails motor impairment, discoordination, or autonomic dysregulation. It is critically important for the neurologist to assess the patient's mechanics to the extent possible within the scope of consultative or ongoing neurologic care. Ergonomics and prosthetics including adaptive work furnishings, braces, specialized footwear, and assistive devices may be crucial for continued vocational engagement. Neurologists can work with physical, occupational, and recreational therapists, as well as podiatrists, prosthetists, and social workers, among others. It is important to distinguish impairment (which physicians assess) from disability (which disability boards assess) and to help the patient distinguish being impaired in a specific life role (eg, school bus driver, spouse, caregiver) from complete and total disability. If it is not possible for the patient to continue to work in their chosen career, it may be necessary to have an open conversation about the patient's domains of preserved function and career interests and look for potential areas of fruitful overlap. This is not the first choice, but for some patients, permanent disability is not an inevitable outcome, and evidence indicates that vocational engagement has a long-term positive impact on chronic pain.[109,110]

MANAGEMENT

The first key to managing pain is ensuring that pathologic factors are addressed to the extent necessary and possible. In many situations, pain serves an essential signaling function, indicative of pathology or a need for treatment. This fact is sometimes overlooked in the pain literature, which tends to focus on high-impact (high-utilization) chronic pain. With a differential diagnosis established and a workup in progress, it is also important to attend to symptomatic pain treatments from the first encounter.

Pharmacologic and nonpharmacologic management are both important to optimize pain control while minimizing problematic side effects. For some patients, oral medication may be sufficient to address a particular problem. For those patients for whom single-agent or dual-agent therapy is insufficient, or when side effects are problematic, it becomes more important to introduce the possibility of integrating pharmacologic and nonpharmacologic therapies. By the time a patient is referred to a neurologist, basic treatment approaches have often already failed to alleviate the patient's pain. For patients for whom pain interventional therapy is viewed as most appropriate, the primary care provider will often refer directly to a pain management specialist. A major reason to favor management that proactively incorporates nonpharmacologic approaches is that most pain medications can cause sedation and some degree of cognitive impairment; nonpharmacologic therapies may improve sleep quality, physical function, and quality of life while not having negative impacts on cognition.[111] In some settings, medication-based solutions continue to be the most common as patients have limited access to, limited capacity for, and financial barriers to nonpharmacologic therapies.[112]

The neurologist confronted with managing pain will want to employ an evidence-based approach to the greatest extent possible.[113] Prescription medications used for the management of chronic and neuropathic pain include pain-active antidepressants and pain-active anticonvulsants (including gabapentinoids). All pain-active antidepressants carry a boxed warning for suicidality risks, and these should be explained to patients and instructions for how to respond in the event of suicidal ideation should be provided. In most cases, the neurologist will want to begin pain-active antidepressants at a low dose and titrate up the dose over several weeks. Pain-active anticonvulsants include gabapentin, which was originally developed to mimic γ-aminobutyric acid (GABA) but was found to not affect GABA receptors in vivo. However, it was released as an adjunctive anticonvulsant and later demonstrated to have benefit as a pain treatment, with strong evidence for efficacy in postherpetic neuralgia and painful diabetic peripheral neuropathy. The development of pregabalin offered another alternative in the same chemical class. Carbamazepine and oxcarbazepine are used as first-line treatment for trigeminal neuralgia, and other anticonvulsants may be used for specific neuropathic pain diagnoses.

Cannabinoids remain experimental and may carry specific health harms, including, as for many pain-active medications, a risk of driving impairment.[114,115] The use of opioids and opioidlike agents for the management of chronic noncancer pain has decreased since the publication of the first set of Centers for Disease Control and Prevention (CDC) guidelines on opioid prescribing in 2016; an updated version of these guidelines was published in 2022.[16,21,116] Neurologists may find it helpful to learn about topical options for the treatment of focal neuropathic pain; in many locales, over-the-counter and compounded topical preparations offer an additional therapeutic tool for patients.

Systematic reviews, recommendations, and guidelines for nonpharmacologic therapies for pain-associated conditions managed in neurology practice continue to accrue evidence of measurable benefits. Current meta-analyses primarily pertain to headache and musculoskeletal conditions, with more limited data for neuropathic conditions. An assessment of the utility of nonpharmacologic therapies for common pain-associated conditions was undertaken by Skelly and colleagues[9,117] and published in 2017 and 2018. They focused on a specific set of common conditions, including: nonspecific low back pain; cervicalgia; knee, hip, and shoulder pain; tension-type headache; and fibromyalgia. Skelly and colleagues[9,117] reviewed a massive body of literature to identify the effect size and quality of evidence for a variety of nonpharmacologic therapies for pain intensity and functional interference, including physical activity (many with active physical therapy direction), massage, mind-body therapies such as yoga and tai chi, clinical psychology treatment, manual therapy, and others. Their review demonstrated that for back pain and other common (non-neuropathic) pain conditions, many therapies have at least some benefits in the short and medium terms, with insufficient evidence to support sustained benefits. Chou and colleagues[113] concurrently examined the evidence in support of medication-based therapy for chronic pain, including low back pain, and found very modest short-term and medium-term benefits and little substantive evidence of long-term benefits.

KEY POINTS

- **Disability related to pain can be the most important aspect of a patient's experience of pain. For some patients, pain entails motor impairment, dyscoordination, or autonomic dysregulation.**
- **Pharmacologic and nonpharmacologic management are both important to optimize pain control while minimizing problematic side effects.**
- **All pain-active antidepressants carry a boxed warning for suicidality risks; these should be explained to patients and instructions for how to respond in the event of suicidal ideation should be provided.**
- **Nonpharmacologic therapies for pain-associated conditions managed in neurology practice continue to accrue evidence of measurable benefits.**
- **Physical activity is important for many reasons, including the upregulation of endogenous analgesic mechanisms and preservation of function, and psychological support is important to reduce pain-related interference with function, suffering, and pain intensity.**
- **Incorporating coordinated nonpharmacologic therapies can reduce pharmacologic focus and polypharmacy, which is associated with cognitive interference and increased falls in older adults and accidental injury, substance use disorders, and long-term dependency in passive pain relief strategies.**

The coordination of treatment options is an important aspect of modern neurologic practice and is not unique to pain-focused care. Cognitive disorders, movement disorders, and other neurologic conditions benefit from "comprehensive" management that selectively incorporates evidence-based therapies. In pain management, there are specific therapeutic domains that are especially relevant. Physical activity is important for many reasons, including the upregulation of endogenous analgesic mechanisms and preservation of function, and psychological support is important to reduce pain-related interference with function, suffering, and pain intensity. Mind-body therapies including yoga and tai chi have demonstrable benefits for several forms of pain, as do specific types of meditation and healthful nutrition. Ergonomics and prosthetics are essential for many patients with pain-associated conditions and should be incorporated proactively into treatment plans. Sleep has a profound association with pain, and efforts to improve sleep can reduce pain impact and severity. Surgical and interventional approaches may be needed; neuromodulating medications should be rationally incorporated into the treatment plan, with evidence-based therapies being selected first, and over-the-counter oral medicines and other preparations may be useful. It is necessary to adapt the selections in these domains for each type of pain, as illustrated in **TABLE 1-3**.[118-122] Incorporating coordinated nonpharmacologic therapies can reduce pharmacologic focus and polypharmacy, which is associated with cognitive interference and increased falls in older adults and accidental injury, substance use disorders, and long-term dependency in passive pain relief strategies.

Interprofessional collaboration is a model of care that aligns especially well with managing pain through the coordination of treatment options.[89] By working with collaborating providers (eg, physical therapists and clinical psychologists), patients will make important and helpful connections that foster a proactive dynamic toward pain, including increased pain self-efficacy.[30,87,123] Physical therapists are especially effective in coaching patients to take charge of pain; clinical psychologists implement evidence-based methods of helping patients gain control over pain; and pharmacists, nurse practitioners and nurse educators, chaplains, nutritionists, and social workers all contribute professional perspectives and support patients in acquiring knowledge and skillfulness in pain self-management. Pain self-management alone may not be sufficient to control a severe pain problem, but pain medications alone may provide less robust and durable clinical benefits than desired, and coordinated management is essential for quality of life and function.

Approaches may vary according to patient characteristics, especially when pain is chronic and severe. For patients with busy work schedules or limited access to transportation, therapies that require attendance at multiple daytime sessions become less feasible. For patients with cognitive impairment, it may be necessary to sequence therapies rather than propose concurrent implementation of multiple therapies at once.

CONTEXT OF TREATMENT

Neurologists can function as consultative members of the pain team or as team leaders. There is evidence that pain rates are rising, and this is likely compounded by the aging population. The future of pain management may see more neurologic involvement in pain care. Neurologists bring a special skill set with advanced training in neurologic localization, familiarity with issues pertaining to

Examples of Coordinated Management of Common Pain-associated Conditions

TABLE 1-3

Therapeutic domain	Conditions		
	Low back pain	Lumbar radiculopathy	Distal symmetrical peripheral neuropathy (hyperglycemic)
Physical activity	Remain as active as possible, may need physical therapy (PT) for neuromuscular retraining[9,117]	Limit initially as activity may exacerbate nerve and disk pain; PT for palliation and rehabilitation	Remain active to help moderate blood sugar; avoid impact as this may worsen foot pain; consider PT for fall prevention
Psychological support	If self-limited: relaxation, guided imagery; if chronic: cognitive behavioral therapy (CBT)[9,116]	Situationally dependent: eclectic, CBT, stress management, activity pacing	Acceptance and commitment therapy or CBT
Mind and body therapies including nutrition	Gentle yoga or tai chi, meditation, healthful nutrition to support weight reduction[9,117]	Yoga: modified and supervised (eg, chair yoga) as tolerated; tai chi as tolerated	Gentle yoga or tai chi, meditation, nutrition counseling to avoid concentrated sugars
Ergonomics and prosthetics	Lumbar support, improved footwear	Lumbar roll, leg bolster, footwear	Diabetic footwear as needed, podiatry
Sleep	Consider heating pad (on medium) for comfort, may need mattress topper	Use leg bolster to reduce spinal pressure; daytime recumbency breaks using bolster	Keep feet cool at night as warming increases pain signaling; time medication for bedtime pain relief
Rescue therapies	Some patients may be candidates for interventional treatments based on underlying pathophysiology[118]	Lumbar steroid injection may yield modest short-term pain relief[119]; if neurologic deficits are present or pain is unmanageable, consider surgical management[118]	For poorly controlled neuropathic pain, consider addition of transcutaneous electrical nerve stimulation or spinal cord stimulation[120,121]
Neuromodulating medications (including pain-active antidepressants, gabapentinoids, and topical agents such as local anesthetics)	May be beneficial if pain is greater than mild and persistent	May be needed to manage pain; can be incorporated as part of a multimedication regimen to address neuropathic, nociceptive (disk tear if present), and inflammatory components of pain	May be needed to manage pain, as pain may be moderate-to-severe and is typically persistent; consider use of pain-active antidepressants or gabapentinoids; topical lidocaine for focal pain
Over-the-counter (OTC) and standard analgesia	OTC medications are typically recommended; avoid long-term use; avoid opioids; avoid oral steroids; consider OTC topicals[113]	Likely that OTC medications are only minimally effective; avoid opioids; single-dose or short-course oral steroids may provide modest short-term benefit[122]	OTC analgesia is unlikely to be effective; due to expectation of longer pain persistence, opioids should be avoided

impairment and disability, and expert knowledge of several medications used for chronic pain.

The US population is facing major challenges in terms of population aging and the pervasive impacts of opioids and other substance use disorders. Most older adults have at least one pain-associated condition, and pain-associated conditions are associated with impairments in mobility and functional independence. Virtually all older adults with opioid use disorder have at least one pain-associated condition and rates of substance use in older adults are rising, meaning that neurologists will be seeing more patients with general neurologic conditions complicated by concurrent pain and substance use disorders.[100] Coordinated pain management and interprofessional collaboration are essential for these patients (**FIGURE 1-1**).

The current state of pain management has developed over several decades of concerted efforts to improve the understanding and treatment of pain in all areas of health care. Pain was documented in some of the earliest extant human writings, and ancient systems of pain regulation—especially meditation, yoga, acupuncture, and qigong—have developed over millennia. Evidence suggests that access to pharmacologic anesthetics was sharply limited before the modern era. With the advent of microscopy, early scientists such as René Descartes and Robert Remak identified the neural structures, in particular C-fibers, that subsume pain transmission from the peripheral to the central nervous system.[124,125]

The development of some anesthetics had a perilous early history, including the misuse of cocaine and heroin, which were initially described as "safe."[126] The study of ballistic injuries experienced during the American Civil War led Silas Weir Mitchell[127] to describe causalgia (more recently termed complex regional pain syndrome) and related chronic neuropathic pain conditions. The lack of safety controls in patent medicine preparations, many consumed by those seeking pain relief, led to the creation of the US Food and Drug Administration (FDA) in the early 1900s. By the middle of the 20th century, Kenneth Keele[128] and others were systematically documenting patients' pain reports using systematic methods. Scientifically, Alan Hodgkin and Andrew Huxley[129] elucidated the mechanisms of action potential propagation essential to nociceptive (and all) neural processing. In the latter half of the 20th century, Barbara Travell systematized the study of referred pain and muscular "knots" arising in patients with visceral ischemia, later publishing the landmark description of myofascial trigger points with David Simon.[54] John Bonica and colleagues[24] formed the IASP in 1975, catalyzing growth in basic, translational, and clinical pain research around the globe from that time onward. The systematic classification of headache disorders, starting with the first edition of the ICHD published in 1988, had a major role in advancing headache and facial pain clinical care and science, which arose from an earlier classification published in the 1960s. Peter Dyck and John Griffin[129-131] contributed to understanding the pathophysiology of peripheral neuropathy. The fall of multidisciplinary pain clinics due to insurance constraints and the resistance of medical schools to incorporating pain as part of the standard curriculum presented substantive and persistent systemic barriers to improvements in pain care.[132]

Pain clinicians began to widely champion the use of the numerical rating scale for rapid clinical pain assessment in the mid-1990s; at the same time, pharmaceutical companies were strategizing to market opioid medications for

wider use against pain, breaking the long-standing taboo that limited opioids to use in those with terminal cancer pain.[133] The publication of a major report for the National Academy of Science, Engineering, and Medicine in 2011, "Relieving Pain in America," was initially hailed but later met with criticism as some began to associate the dramatic increases in prescription opioid use with the well-intentioned efforts to assess and treat pain with knowledge and compassion, as mandated by the Joint Commission.[134,135] Prescription opioids undoubtedly contributed to the deaths of many thousands of Americans.[116] The CDC opioid guidelines published in 2016 led to a reduction in opioid prescriptions in the United States, and there is evidence that rapid opioid tapering carries increased risks for suicide and mental health deterioration.[103] Meanwhile, the global context of end-of-life pain management continues to be characterized by extremely limited access to prescription opioids.[136] The National Institutes of Health (NIH) is currently investing millions of dollars into pain research, promising improved pain care in the future. The efforts to advance pain science and clinical care have continued on many fronts and include innumerable studies, systematic reviews of pharmacologic and nonpharmacologic therapies, and a new era of patient and caregiver empowerment and access to resources to improve pain care.[137]

KEY POINTS

- **By working with collaborating providers (eg, physical therapists and clinical psychologists), patients will make important and helpful connections that foster a proactive dynamic toward pain, including increased pain self-efficacy.**
- **Neurologists bring a special skill set to pain management, with advanced training in neurologic localization, familiarity with issues pertaining to impairment and disability, and expert knowledge of several medications used for chronic pain.**

CONCLUSION

Several decades of clinical program building and research, from basic science to meta-analysis studies, have established an integrated pain system with fascinating pathophysiologic features and protean impacts on clinical outcomes and society. A systematic approach to pain clinical care is highly effective and ideally incorporates knowledge, skills, and compassion. A degree of formal training in pain assessment, classification, diagnosis, and management, together with the ability to navigate limitations in health system capacities, the determination to maximize care through interprofessional collaboration, and meaningful responses to the need for advocacy for those affected by social determinants of health are all necessary to improve outcomes. Extensive evidence supports the use of comprehensive pain treatment strategies, which may include pain self-management, integrative, complementary, and whole-health approaches in coordination with pharmacologic and interventional strategies. Exceptional pain care relies on a strong therapeutic alliance between the patient, their caregivers and family members, and clinicians, among whom the neurologist may serve a vital role.

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